METHODS OF SYNTHESIZING OLIGONUCLEOTIDES USING CARBONATE PROTECTING GROUPS AND ALPHA-EFFECT NUCLEOPHILE DEPROTECTION

ABSTRACT OF THE DISCLOSURE

The invention provides methods for synthesizing oligonucleotides using nucleoside monomers having carbonate protected hydroxyl groups that are deprotected with α-effect nucleophiles. The α-effect nucleophile irreversibly cleave the carbonate protecting groups while simultaneously oxidizing the internucleotide phosphite triester linkage to a phosphodiester linkage. The procedure may be carried out in aqueous solution at neutral to mildly basic pH. The method eliminates the need for separate deprotection and oxidation steps, and, since the use of acid to remove protecting groups is unnecessary, acid-induced depurination is avoided. Fluorescent or other readily detectable carbonate protecting groups can be used, enabling monitoring of individual reaction steps during oligonucleotide synthesis. The invention is particularly useful in the highly parallel, microscale synthesis of oligonucleotides.